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(19) (CA) APPLICATION FOR CANADIAN PATENT (12)

(54) Blends of Glycolide and/or Lactide Polymers and
Caprolactone and/or Trimethylene Carbonate Polymers and
Absorbable Surgical Devices Made Therefrom

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Notice: This application is as filed and may therefore contain an
incomplete specification.

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**BLENDS OF GLYCOLIDE AND/OR LACTIDE POLYMERS AND
CAPROLACTONE AND/OR TRIMETHYLENE CARBONATE POLYMERS
AND ABSORBABLE SURGICAL DEVICES MADE THEREFROM**

BACKGROUND OF THE INVENTION

This invention relates to glycolide and/or lactide based polymer compositions and more particularly to polymer compositions which are blends of a glycolide and/or lactide homopolymer or glycolide/lactide copolymer and polycaprolactone homopolymer and/or polytrimethylene carbonate homopolymer and/or caprolactone or trimethylene carbonate copolymer, said polymer compositions being particularly useful in the manufacture of absorbable surgical devices.

Polymers and copolymers of, and surgical devices made from, lactide and/or glycolide and/or related compounds are well-known. See, e.g., U.S. Patent Nos. 2,668,162, 2,683,136, 2,703,316, 2,758,987, 3,225,766, 3,268,486, 3,268,487, 3,297,033, 3,422,181, 3,442,871, 3,463,158, 3,468,853, 3,531,561, 3,565,869, 3,597,449, 3,620,218, 3,626,948, 3,636,956, 3,736,646, 3,739,773, 3,772,420, 3,773,919, 3,781,349, 3,784,585, 3,792,010, 3,797,499, 3,839,297, 3,846,382, 3,867,190, 3,875,937, 3,878,284, 3,896,802, 3,902,497, 3,937,223, 3,982,543, 4,033,938, 4,045,418, 4,057,537, 4,060,089, 4,137,921, 4,157,437, 4,243,775, 4,246,904, 4,273,920, 4,275,813, 4,279,249, 4,300,565, and 4,744,365, U.K. Pat. or Appln. Nos. 779,291, 1,332,505, 1,414,600, and 2,102,827, D.K. Gilding et al.,

resistance to thermal distortion of poly(lactide/glycolide) surgical devices without adversely affecting their rate of loss of tensile strength. More particularly, the compositions of U.S. Patent No. 4,744,365 comprise a multi-phase polymeric composition derived from lactide and glycolide, the first phase having about 0 to about 25% m glycolide moieties and about 75 to about 100% m lactide moieties and the other phases having glycolide and lactide moieties in amounts such that the composition overall has up to 45% m glycolide moieties, wherein the first phase constitutes at least 50% (and preferably not more than about 95%) by weight of the composition.

In addition to the afore-recited patents and other documents which disclose polymers and copolymers of, and surgical devices made from lactide and glycolide, other patents disclose surgical devices prepared from copolymers of lactide or glycolide and other monomers including caprolactone or trimethylene carbonate. Such patents include U.S. Patent No. 4,700,704, U.S. Patent No. 4,605,730 and U.S. Patent No. 4,643,734. More particularly, U.S. Patent No. 4,605,730 and U.S. Patent No. 4,700,704 disclose copolymers of epsilon-caprolactone and glycolide useful in making surgical articles and particularly surgical sutures having low Young's modulus. In addition to the afore-recited patents, U.S. Patent No. 4,624,256 discloses the utilization of high molecular weight caprolactone polymers as coatings for surgical sutures, while U.S. Patent No. 4,429,080 discloses surgical articles manufactured from triblock copolymers prepared from copolymerizing glycolide with trimethylene carbonate.

1 afore-described polymer blend compositions of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Copending U.S. patent application Serial No.

5 07/654,234 filed on February 12, 1991 discloses a bioabsorbable reinforced composite material and method for the production thereof, wherein a component of the composite material may comprise a blend of homopolymers or copolymers of glycolide and lactide and polycaprolactone, and/or
10 polytrimethylene carbonate.

In accordance with the present invention, it has now been found that absorbable surgical devices manufactured from these blends comprised of glycolide homopolymer, lactide homopolymer, glycolide/lactide copolymer or mixtures
15 thereof and polycaprolactone homopolymer, polytrimethylene carbonate homopolymer and/or copolymers of caprolactone or trimethylene carbonate and glycolide and/or lactide, wherein the caprolactone or the trimethylene carbonate is the predominant monomer, possess improved physical and
20 mechanical properties in comparison with surgical devices derived from glycolide or lactide homopolymer or glycolide/lactide copolymer alone.

More particularly, surgical devices prepared from the polymer blends of the present invention comprising
25 glycolide or lactide homopolymer or glycolide/lactide copolymer and polycaprolactone or polytrimethylene carbonate homopolymer and/or copolymers of caprolactone or trimethylene carbonate and glycolide and/or lactide, wherein the caprolactone or the trimethylene carbonate is the
30 predominant monomer (i.e. greater than 50 mole percent preferably at least 80 mole percent), are found to exhibit

1 useful in the practice of the present invention are those
comprising about 18/82 glycolide/lactide (mole percent),
10/90 glycolide/lactide (mole percent) 35/65 glycolide/
5 lactide (mole percent) and 42/58 glycolide/lactide (mole
percent).

The glycolide homopolymers, lactide homopolymers
and glycolide/lactide copolymers employed in the blends of
the present invention are known materials and are readily
synthesized by known methods. Generally, the glycolide
10 and/or lactide homopolymer and glycolide/lactide copolymers
employed in the blends of the present invention have a
molecular weight such that they have an inherent viscosity
of from about 0.9 to about 2.0 dl/g and preferably about 1.0
to about 1.8 dl/g measured at 30°C at a concentration of
15 0.25 g/dl in chloroform or hexafluoroisopropanol (HFIP).
Particularly preferred glycolide/lactide copolymer for the
purposes of the present invention are the two-phase or
multi-phase compositions disclosed in U.S. Patent No.
4,744,365, the entire contents of which is incorporated by
20 reference herein.

The polycaprolactone homopolymers and copolymers
employed in polymer blends of the present invention are also
well known and commercially available materials. For the
purposes of the present invention, polycaprolactone
25 homopolymers or copolymers having an inherent viscosity of
from about 0.8 to about 2.5 dl/g measured at 30°C and a
concentration of 0.25 g/dl in chloroform or HFIP are
generally employed.

The polytrimethylene carbonate homopolymers and
30 copolymers used in the practice of the present invention are
also well known and commercially available materials. For

1 preferably, by injection molding the blend at temperatures
in the range of from about 300 to about 400°F at an
injection molding pressure of, for example, about 1,500 psi.
Typically, the feed for the injection molding apparatus is a
5 melt blend of the two polymers in pellet form. The polymers
should be quite dry when being injection molded in order to
avoid hydrolytic degradation during processing. After
molding, the surgical devices can be packaged and sterilized
by conventional procedures. It may be desirable to anneal
10 the devices to remove residual stresses and strains, to
stabilize the shape of the device, and to reduce or
eliminate defects in the piece. Annealing typically
comprises reheating the polymeric device to above its glass
transition temperature where chain mobility is greatest, and
15 then slowly and gradually cooling the device to avoid
reintroducing. Procedures, conditions and apparatus for
annealing polymeric structures are well known in the art.

A wide variety of absorbable surgical devices can
be manufactured from the polymer blends of the present
20 invention. These include fasteners, such as staples, clips
and the like and other implant devices, such as pins, bone
screws, or the like.

As expressed hereinbefore, the surgical devices of
the present invention exhibit excellent in vivo cyclic flex
25 performance, a mechanical property which is highly desired
in surgical devices and in particular, for example, in
surgical implant devices, such as surgical fastener/retainer
systems which, after implantation, are subject to a variety
of forces and often undergo repeated flexing.

30 Furthermore, surgical devices manufactured from
the novel polymer blends of the present invention exhibit

Example 1

A copolymer of glycolide and lactide is prepared as follows:

Hydroxyacetic acid (glycolic acid) is heated under nitrogen to 180°C to remove impurities such as water. Pressure is then reduced and heating is continued for two hours to yield a prepolymer of polyglycolic acid, which is recovered and powdered.

The prepolymer is heated in the presence of Sb_2O_3 at 275°C under low pressure with an argon purge and stirring. The prepolymer cracks and glycolide is distilled over and recovered in a cold vacuum receiver. Preferably, the glycolide is purified by conventional techniques, such as distillation, crystallization, and sublimation.

L-lactide is used alone or in combination with a small amount of the DL racemer. L-lactide is purified by crystallization from toluene solution. The DL racemer, if used, is purified by crystallization from ethyl acetate.

A mixture of the purified glycolide (18 mole percent) and lactide (82 mole percent) is charged to a reactor under an argon blanket. A solution of stannous octoate catalyst in diethyl ether is added to give 0.02% w. of catalyst, based on the total weight of glycolide and lactide. The reactor is further purged with argon and held at 5 psi while heating to 170°-175°C. Pressure and temperature are maintained for six hours.

The reaction product is isolated, comminuted, and treated to remove residual reactants. Any method capable of removing the unreacted monomers from the crude reaction product may be used. A preferred purification procedure is as follows.

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the glycolide/lactide copolymer (18/82) described above in the reactor at a temperature of 190°C and at a weight ratio of 25:75. The blended polymer is extruded, ground, extracted with ether, and dried in accordance with known procedures.

Surgical devices fabricated from this blended polymer exhibit excellent physical properties, including good impact resistance, resistance to crazing and cyclic flexibility.

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Example 3

The test plates injection molded as described in Example 2 are tested for impact resistance using a standard dart impact tester. The test plates are designated as follows:

Control: glycolide/lactide copolymer (18/82); unannealed

Sample 1: glycolide/lactide copolymer (18/82) blended with polycaprolactone at a weight ratio of 85:15; unannealed

Sample 2: glycolide/lactide copolymer (18/82) blended with polycaprolactone at a weight ratio of 85:15; annealed

Sample 3: glycolide/lactide copolymer (18/82) blended with polycaprolactone at a weight ratio of 80:20; unannealed

Sample 4: glycolide/lactide copolymer (18/82) blended with polycaprolactone at a weight ratio of 80:20; annealed

The results of the impact tests are set forth in the following Table I:

TABLE I

Force (in-lb)	Control	Sample 1	Sample 2	Sample 3	Sample 4
10	4	4	4	4	3
20	6	4	4	4	3
30			6		
40				5	4

Mode of Failure: 1. No effect; 2. Slight fractures;
3. Indentation with some crazing;
4. Cracks at point of contact; 5. Hole punched at point of contact; 6. Shattered.

Example 4

A two-phase polymeric composition comprising glycolide and lactide is prepared according to the procedure described in U.S. Patent No. 4,744,365. A first monomer mixture of glycolide and lactide at a mole ratio of 10:90 is polymerized in the presence of a stannous octate catalyst until the polymerization is substantially complete. To this glycolide/lactide copolymer is added a second monomer mixture consisting of additional glycolide, such mixture being added in sufficient quantity that the final mole ratio of the two-phase polymeric composition is 35:65 glycolide to lactide. After the additional glycolide polymerizes with the glycolide/lactide copolymer, the two-phase polymer composition is ground, dried and ether extracted in accordance with known procedures.

Polycaprolactone is combined with the two-phase glycolide/lactide polymeric composition at mole ratios of 5:95 and 10:90, melt blended therewith at a temperature of 170°C to 200°C and the resulting blends are pelletized for subsequent use as described below.

The pellets of melt blended polymer are injection molded at a temperature of 130°C to 140°C at an injection molding pressure, e.g., 1,500 to 1,750 psi, to form a series of test plates measuring 2.2 inch x 2.7 inch x 0.070 inch. Control test plates are also injection molded from the two-phase glycolide/lactide polymeric compositions. One portion of the test plates are annealed at an annealing temperature of about 85°C to 100°C for 12 to 16 hours to remove internal stresses. A second portion of the test plates are not annealed.

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TABLE II

Force (in-lb)	Control 1	Control 2	Sample 1	Sample 2	Sample 3	Sample 4
10	4 5	4				
20	5	4 5	4	2 4 2	2	2
30			5			
40	5 6	5 6		4	3	3
50	5 6					
60	6	6		4 4	3	3
80				4 4	3	3 3 3

These results show that the polymeric blends of the present invention exhibit improved impact resistance as compared to non-blended controls, i.e., glycolide/lactide polymers without added polycaprolactone. In addition, the test plates for Samples 1-4 exhibit improved resistance to crazing. Improved cyclic flex performance is also to be expected.

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1 5. The polymer composition of Claim 1 wherein
component b) is selected from the group consisting of
polycaprolactone homopolymer and polytrimethylene carbonate
homopolymer.

5 6. The polymer composition of Claim 1 wherein the
glycolide/lactide copolymer has an inherent viscosity of
from about 0.9 to about 2.0 dl/g measured at 30°C at a
concentration of 0.25 g/dl in chloroform or
10 hexafluoroisopropanol.

7. The polymer composition of Claim 5 wherein
said polycaprolactone homopolymer has an inherent viscosity
of from about 0.8 to about 2.5 dl/g measured at 30°C at a
15 concentration of 0.25 g/dl in chloroform or hexafluoro-
isopropanol and said polytrimethylene carbonate has an
inherent viscosity of from about 0.8 to about 2.5 dl/g
measured at 30°C at a concentration of 0.25 g/dl in
chloroform or hexafluoroisopropanol.

20 8. The polymer composition of Claim 2 wherein the
glycolide/lactide copolymer comprises a multi-phase
composition, the first phase having from about 0 to about 25
mole percent glycolide moieties and about 75 to about 100
25 mole percent lactide moieties and the other phase or phases
having glycolide and lactide moieties in amounts such that
the composition overall has up to 45 mole percent glycolide
moieties, wherein the first-phase constitutes at least 50%
by weight of copolymer.

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